

## DETAILED DESCRIPTION

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[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the optical aging depressant which has the outstanding optical aging depressor effect over the skin, such as improving the optical degraded phenomenon resulting from chronic exposure of daylight about the skin external preparations containing an optical aging (optical aging) depressant and it, and the skin external preparations containing it.

[0002]

[Description of the Prior Art] Before, medicinal properties are added to skin external preparations, such as a milky lotion, cream, face toilet, a pack, a charge of washing, an essence, dispersion liquid, ointment, and liquids for external use, for the purpose of giving these predetermined drug effect. For example, vitamin A etc. are added in order to improve the wrinkles of the skin produced by ultraviolet-rays exposure, such as aging and daylight, and slack.

[0003]

[Problem(s) to be Solved by the Invention] However, such skin external preparations are not enough as the anti-aging effect, or it deteriorates in pharmaceutical preparation, expected drug effect is not obtained in many cases, and the improvement was desired.

[0004]

[Means for Solving the Problem] This invention persons found out having optical aging depressant action with a high ingredient which has singlet oxygen elimination ability, as a result of examining wholeheartedly what can be used as an anti-aging ingredient of skin external preparations. And these ingredients could be blended with skin external preparations as an aging prevention ingredient, and by combining with other medicinal properties, found out that an effect outstanding as skin external preparations was acquired, and completed this invention.

[0005] That is, skin external preparations which have outstanding optical antiaging effects, wherein this invention contains an optical aging depressant and it which have singlet oxygen elimination ability are provided.

[0006] Ingredient [ following ] (A) This invention reaches (B).

(A) Provide skin external preparations containing a kind of a drug effect agent chosen from a kind of the optical aging depressant according to claim 1 or a two or more sort (B) anti-oxidant, an anti-inflammatory agent, a chelating agent, and ultraviolet inhibitor, or two sorts or more.

[0007]

[Embodiment of the Invention] The optical aging depressant as an ingredient which has the singlet oxygen elimination ability used for this invention, A lycopene, lutein, B-carotene, astaxanthin, mannitol, Rutin, rutin glucoside, quercetin, L-histidine, acetylation L-histidine, Histamine, sulfur containing amino acid, phospholipid, erythorbic acid, tryptophan, Tyrosine, methionine, cystine, a hypotaurine, thiotaurine, zeaxanthin, vitamin E, the derivative of the above-mentioned ingredient, and a salt are mentioned, and an origin substance in particular is specified about neither a synthetic method, nor extraction and a purification method.

[0008] Although the Spatholobus suberectus Dunn extract, a ginseng extract, a mica cuttlefish extract, a SAMPENZU extract, the Melissa extract, a YASHAJITSU extract, a creeping saxifrage extract, a rakanka extract, a tea extract, etc. are mentioned, the optical aging depressant as a vegetable extract which

has the singlet oxygen elimination ability used for this invention, In manufacturing the extract used for this invention, in particular the kind or origin are not limited. An extract is extracted from what performed juice or distillation extraction or dried this vegetation using a suitable extracting solvent. The solvent in particular is not limited but is extracted using various solvents etc. which are shown below. [0009]as an extracting solvent -- water and low-grade monohydric alcohol (methyl alcohol.) Ethyl alcohol, 1-propanol, 2-propanol, 1-butanol, liquefied polyhydric alcohol (glycerin and propylene glycol.), such as 2-butanol Lower alkyl ester, such as a 1,3-butylene glycol (ethyl acetate etc.), Hydrocarbon (benzene, hexane, pentane, etc.), ketone (acetone, methyl ethyl ketone, etc.), ether, acetonitrile (diethylether, a tetrahydrofuran, dipropyl ether, etc.), etc. are mentioned, and a kind or two sorts or more can be used. It can be made to be able to dissolve in arbitrary solvents and an extract can also be used, after using it as it is or making it evaporate to dryness.

[0010]Although the optical aging depressant of this invention can obtain skin external preparations by blending those kinds or two sorts or more with the base of various gestalten used for the usual skin external preparations, and pharmaceutical-preparation-izing them, Skin external preparations with the more outstanding anti-aging effect are obtained by combining with medicinal properties, such as an anti-oxidant, an anti-inflammatory agent, a chelating agent, and ultraviolet inhibitor.

[0011]as an anti-oxidant -- retinol and its derivative (retinol palmitate.) Vitamin A, such as retinals, such as retinol acetate, and a derivative of those, and dehydroretinal. Pyridoxine (pyridoxine hydrochloride, pyridoxine dioctanoate, etc.). other vitamin B, the derivative of those and those salts, and nicotinic acid (nicotinamide.) Vitamin E, its derivative, and those salts, such as nicotinic acid benzyl, Dibutylhydroxytoluene (BHT), butylhydroxyanisole (BHA), its derivative, and those salts, Carotenoid, such as carotene and astaxanthin, phospholipid, quercetin, Quercitrin, a Scutellaria root extract, a ginkgo tree extract, a ginseng extract, the Melissa extract, a creeping saxifrage extract, a GOKAHI extract, a YASHAJITSU extract, the other plant extracts that contain flavonoid in an ingredient, etc. are mentioned.

[0012]As an anti-inflammatory agent, chondroitin sulfate and its derivative, allantoin, An Arnica extract, a St. John's wort extract, a cork tree bark extract, a Lonicera-japonica-thunb extract, A watercress extract, a comfrey extract, a salvia extract, a lithospermi radix extract, A Betula-alba extract, the Calendula officinalis extract, a sambucus extract, a HOOU extract, A Sapindus mukurossi extract, a eucalyptus extract, the Astragalus sinicus extract, glycyrrhizic acid, glycyrrhetic acid, those derivatives and those salts, an aloe extract, perilla exttact, mugwort extract, a chamomile extract, etc. are mentioned.

[0013]As a chelating agent, citrate, sodium acid citrate, potassium citrate, Tartaric acid, the sodium tartrate, potassium tartrate, a potassium sodium tartrate, Gluconic acid, phytic acid, sodium phytate, potassium phytate, Sodium polyphosphate, sodium metaphosphate, desferrioxamine, diethylenetriamine penta- SECHIKKU acid, o-phenanthrolin, transferrin, ferritin, lactoferrin, caffeic acid, maltol, purpurogallin, pyrogallol, etc. are mentioned.

[0014]As ultraviolet inhibitor, Para methoxycinnamic acid-2-ethylhexyl, oxybenzone, 4-tert-butyl-4'-methoxy-dibenzoylmethane, titanium oxide, particulate titanium oxide, a zinc oxide, etc. are mentioned.

[0015]The loadings of the optical aging depressant of the ingredient (A) in the skin external preparations of this invention are 0.00001 - 10 mass % (it is only described as "%" below) preferably, and are 0.0001 to 5% of range more preferably. When using a plant extract with an extract, what is necessary is just this range as a dry solid. If it is this range, the skin external preparations in which the more outstanding optical aging depressor effect is shown will be obtained.

[0016]Although the loadings of the above-mentioned ingredient (B) in the skin external preparations of this invention are different according to the kind of drug effect agent, it is preferred to consider it as the range shown below. When it was this range and combines with the optical aging depressant of an ingredient (A), the temporal stability of the optical aging depressant of the ingredient (A) in pharmaceutical preparation and pharmaceutical preparation cannot be affected, and a higher effect can be demonstrated.

[0017]The loadings of the anti-oxidant in the skin external preparations of this invention are 0.0001 to 3% of range more preferably 0.00001 to 5%. When using a plant extract with an extract, what is necessary is just this range as a dry solid. The skin external preparations in which the more outstanding manifestation of the antioxidation effect will be seen if it is this range, and the outstanding aging depressor effect is shown are obtained.

[0018]As loadings of the anti-inflammatory agent in the skin external preparations of this invention, 0.00001 to 5% of range is preferred, and is 0.0001 to 3% of range more preferably. When using a plant extract with an extract, what is necessary is just this range as a dry solid. The skin external preparations in which the outstanding anti-inflammation effect will be seen if it is this range, and the outstanding aging depressor effect is shown are obtained.

[0019]As loadings of the chelating agent in the skin external preparations of this invention, it is 0.001 to 1% of range more preferably 0.0001 to 3%. The skin external preparations in which the metal blockade effect of having excelled more will be seen if it is this range, and the outstanding aging depressor effect is shown are obtained.

[0020]As loadings of ultraviolet inhibitor in the skin external preparations of this invention, it is 0.001 to 10% of range more preferably 0.0001 to 20%. The skin external preparations in which the more outstanding ultraviolet-rays preventive effect will be seen if it is this range, and the outstanding aging depressor effect is shown are obtained.

[0021]These anti-oxidants, an anti-inflammatory agent, a chelating agent, and ultraviolet inhibitor can be used combining a kind or two sorts or more.

[0022]The skin external preparations of this invention can prepare the (A) ingredient which is an essential ingredient, and the (B) ingredient in accordance with a conventional method as a base of various gestalten known as usual skin external preparations.

[0023]Especially as an example of the combination gestalt of skin external preparations, it is not limited, for example, can be considered as cosmetics, such as a milky lotion, cream, face toilet, a pack, a charge of washing, makeup cosmetics, dispersion liquid, and ointment, external use drugs, etc.

[0024]The ingredient usually used for skin external preparations, such as cosmetics and drugs, according to the gestalt of skin external preparations in addition to the above-mentioned essential ingredient, For example, water (purified water, hot spring water, deep sea water, etc.), oils, a surface-active agent, metal soap, A gelling agent, a granular material, alcohols, a water soluble polymer, a coat formation agent, resin, A clathrate, an antimicrobial agent, PH regulator, a pick-me-up, a circulation accelerator, an astringent, a whitening agent, an antiseborrheic drug, a moisturizer, a keratolytic drug, the ingredient (A) of this invention, vegetation and animals other than (B), and an extract from microorganism, an enzyme, hormone, and vitamins can be added. What is shown below as an example of a suitable ingredient, respectively is mentioned.

[0025]or [ whether it is a natural system oil or that it will be synthetic oil as oils if used for the usual cosmetics ] -- or, Any oils, such as hydrocarbon, lows, fatty acid, higher alcohol, ester oil, silicone oil,

and fluorine system oil, can be used regardless of whether they are a solid, a semisolid, and a fluid and description. For example, squalane, squalene, a ceresin, paraffin, paraffin wax, A liquid paraffin, pristane, polyisobutylene, microcrystallin wax, Hydrocarbon, such as vaseline, yellow bees wax, a carnauba wax, a candelilla low, Lows, such as spermaceti wax, beef tallow, neat's foot lipid, beef bone fat, hardening beef tallow, hydrogenated oil, a turtle oil, Animal oil, such as lard, horse fat, a mink oil, liver oil, and yolk oil, lanolin, liquefied lanolin, Reduction lanolin, lanolin alcohol, hard lanolin, acetic acid lanolin, Lanolin fatty acid isopropyl, POE lanolin alcoholic ether, POE lanolin alcoholic acetate, a lanolin fatty acid polyethylene glycol, Lanolin derivatives, such as POE hydrogenation lanolin alcoholic ether, lauric acid, Myristic acid, pulmitic acid, stearic acid, behenic acid, undecylenic acid, Oleic acid, arachidonic acid, docosahexaenoic acid (DHA), isostearic acid, Fatty acid, such as 12-hydroxystearic acid, lauryl alcohol, myristyl alcohol, palmityl alcohol, stearyl alcohol, behenyl alcohol, hexadecyl alcohol, oleyl alcohol, isostearyl alcohol, A hexyldodecanol, an octyldodecanol, the cetostearyl alcohol, 2-decyltetradeci Norian, cholesterol, a phytosterol, A sitosterol, lanosterol, POE cholesterol ether, Higher alcohol, such as monostearyl glycerin ether (batyl alcohol), Diisobutyl adipate, adipic acid-2-hexyldecyl, adipic acid-di-2-heptylundecyl, Mono- isostearic acid-N-alkyl glycol, isostearic acid isocetyl, Tori trimethylolpropane isostearic acid, di-2-ethylhexanoic acid ethylene glycol, 2-ethylhexanoic acid Sept Iles, tri-2-ethylhexanoic acid trimethylolpropane, Tetra-2-ethylhexanoic acid pentaerythritol, octanoic acid Sept Iles, Octyldodecyl gum ester, oleic acid oleyl, oleic acid octyldodecyl, Oleic acid decyl, neopentyl glycol dicaprates, triethyl citrate, succinic acid-2-ethylhexyl, amyl acetate, ethyl acetate, butyl acetate, stearic acid isocetyl, butyl stearate, diisopropyl sebacate, di-2-ethylhexyl sebacate, Lactic acid Sept Iles, lactic acid Millis Chill, pulmitic acid isopropyl, pulmitic acid-2-ethylhexyl, Pulmitic acid 2-hexyldecyl, pulmitic acid 2-heptylundecyl, 12-hydroxystearyl acid cholesteryl, dipentaerythritol fatty acid ester, Myristic acid isopropyl, myristic acid octyldodecyl, myristic acid-2-hexyldecyl, Myristic acid Millis Chill, dimethyloctanoic acid hexyldecyl, lauric acid ethyl, Lauric acid hexyl, N-lauroyl L-glutamic acid-2-octyldodecyl ester, Ester oil, such as malate diisostearyl, aceto glyceride, TORIISO octanoic acid glyceride, Tori isostearic acid glyceride, Tori Isopar RUMICHIN acid glyceride, Tri-2-ethylhexanoic acid glyceride, monostearin acid glyceride, Glyceride oils, such as di-2-heptylundecanoic acid glyceride and trimyristin acid glyceride, Dimethylpolysiloxane, a methylphenyl polysiloxane, methyl hydrogen polysiloxane, octamethylcyclotetrasiloxane, decamethyl cyclopentasiloxane, A dodecamethyl cyclohexa siloxane, tetramethyl tetrahydrogen cyclotetrasiloxane, Fluorine system oils, such as silicone oil, such as high-class alkoxy denaturation silicone, such as steer ROKISHI silicone, higher-fatty-acid denaturation silicone, silicone resin, silicone rubber, and silicone resin, perfluoro polyether, a perfluoro decalin, and perfluoro octane, are mentioned.

[0026] As a surface-active agent, although there is an active agent of anionic, cationicity, nonionic, and both sexes, As an anionic surface-active agent, fatty acid soap, such as sodium stearate and pulmitic acid triethanolamine, Carboxylate, such as condensation of alkyl ether carboxylic acid and its salt, amino acid, and fatty acid, Alkyl sulfonic acid, an alkene sulfonate, the sulfonate of fatty acid ester, The sulfonate of fatty acid amide, an alkyl-sulfonic-acid salt and the sulfonate of the formalin condensate, Alkyl-sulfuric-acid ester salt, the second class fatty alcohol sulfate, alkyl, and allylethreal sulfate ester salt, The sulfuric ester salt of fatty acid ester, the sulfuric ester salt of fatty acid ARUKI roll amide, Sulfuric ester salt, such as turkey red oil, an alkyl-phosphoric-acid salt, an ether phosphate, An alkyl allyl ether phosphate, an amide phosphate, a N-acylamino acid system active agent, etc.; as a cationic

surface-active agent, Amine salt, such as an alkylamine salt, polyamine, and amino alcohol fatty acid derivatives, alkyl quarternary ammonium salt, aromatic quarternary ammonium salt, a pyridium salt, imidazolium salt, etc.; As a nonionic surfactant, a sorbitan fatty acid ester, A glycerine fatty acid ester, polyglyceryl fatty acid ester, propylene glycol fatty acid ester, Polyethylene glycol fatty acid ester, sucrose fatty acid ester, polyoxyethylene alkyl ether, Polyoxypropylene alkyl ether, polyoxyethylene alkyl phenyl ether, Polyoxyethylene fatty acid ester, polyoxyethylene sorbitan fatty acid ester, Polyoxyethylene sorbitol fatty acid ester, polyoxyethylene glycerine fatty acid ester, Polyoxyethylene propylene glycol fatty acid ester, polyoxyethylene castor oil, Polyoxyethylene hydrogenated castor oil, polyoxyethylene phytostanol ether, Polyoxyethylene phytosterol ether, polyoxyethylene cholestanol ether, Polyoxyethylene cholesteryl ether, polyoxyalkylene denaturation organopolysiloxane, Polyoxyalkylene alkyl covariance organopolysiloxane, alkanol amide, sugar ether, sugar amide, etc.; a betaine, aminocarboxylate, an imidazoline derivative, etc. are mentioned as an ampholytic surface active agent.

[0027]As metal soap, 12-hydroxyaluminum stearate, Zinc stearate, aluminum stearate, calcium stearate, Magnesium stearate, myristic acid zinc, myristic acid magnesium, cetyl-ether-phosphate zinc, cetyl-ether-phosphate calcium, cetyl-ether-phosphate zinc sodium, zinc laurate, zinc undecylenate, etc. are mentioned.

[0028]As a gelling agent, amino acid derivatives, such as N-lauroyl L-glutamic acid, alpha, and gamma-di-n-butylamine, Dextrin pulmitic acid ester, dextrin stearic acid ester, Dextrin fatty acid ester, such as dextrin 2-ethylhexanoic acid pulmitic acid ester, Sucrose fatty acid ester, such as sucrose pulmitic acid ester and sucrose stearic acid ester, Organic modified clay minerals, such as a benzyliene derivative of sorbitol, such as monobenzylienesorbitol and dibenzylienesorbitol, dimethylbenzyl DODESHIRUAMMONIUMU montmorillonite clay, and dimethyldioctadecyl ammonium MOMMORIRONAITOKURE, etc. are mentioned.

[0029]if it is what is used for the usual cosmetics as a granular material -- the shape (a globular shape.) Regardless of a needle, tabular, \*\* and particle diameter (the shape of haze, particles, the paints class, etc.), and particulate structures (porosity, quality of nonporous, etc.), can use anything, for example, as inorganic powder, Magnesium oxide, barium sulfate, calcium sulfate, magnesium sulfate, Calcium carbonate, magnesium carbonate, talc, synthetic mica, mica, kaolin, A sericite, white mica, synthetic mica, phlogopite, lepidolite, black mica, lithia mica, Silicic acid, a silicic acid anhydride, aluminum silicate, a magnesium silicate, the magnesium aluminum silicate, Sulfur-containing aluminum silicate, a calcium silicate, silicic acid barium, silicic acid strontium, Tungstic acid metal salt, hydroxyapatite, a vermiculite, As an organic granular material, a HAIJI light, montmorillonite, zeolite, ceramic powder, calcium diphosphate, alumina, aluminium hydroxide, boron nitride, boron nitride, etc., Polyamide powder, polyester powder, polyethylene powder, polypropylene powder, polystyrene powder, polyurethane, benzoguanamine powder, Polymethyl benzoguanamine powder, tetrafluoroethylene powder, Polymethylmethacrylate powder, silk powder, nylon powder, 12 nylon, 6 nylon, a styrene acrylic acid copolymer, a divinylbenzene styrene copolymer, Polyvinyl resin, urea resin, phenol resin, a fluoro-resin, silicone resin, As a colored pigment, an acrylic resin, melamine resin, an epoxy resin, polycarbonate resin, a micro crystallite textiles granular material, lauroyl lysine, etc., Inorganic brown system paints, such as an inorganic red pigment of iron oxide, iron hydroxide, and titanate iron, and gamma-iron oxide, Inorganic black pigments, such as inorganic yellow system paints, such as yellow oxide of iron and ochre, black oxide of iron, and carbon black, Inorganic purple paints, such as

manganese violet and cobalt violet, chromium hydroxide, Inorganic green pigments, such as chrome oxide, cobalt oxide, and titanate acid cobalt, Prussian blue, As a pearl pigment, what rake-ized inorganic blue system paints, such as ultramarine, and tar system coloring matter, the thing which rake-ized natural coloring matter, the composite powder which composite-ized these granular materials, etc., Titanium oxide covering mica, titanium oxide covering mica, bismuth oxychloride, titanium oxide covering bismuth oxychloride, titanium oxide covering talc, fish scale foil, titanium oxide covering coloring mica, etc., As metal powder paints, as; tar dye, aluminum powder, kappa powder, stainless steel powder, etc., The red No. 3, the red No. 104, the red No. 106, the red No. 201, the red No. 202, The red No. 204, the red No. 205, the red No. 220, the red No. 226, the red No. 227, The red No. 228, the red No. 230, the red No. 401, the red No. 505, the yellow No. 4, The yellow No. 5, the yellow No. 202, the yellow No. 203, the yellow No. 204, the yellow No. 401, The blue No. 1, the blue No. 2, the blue No. 201, the blue No. 404, the green No. 3, the green No. 201, The green No. 204, the green No. 205, the orange No. 201, the orange No. 203, the orange No. 204, the orange No. 206, orange No. 207, etc.; as natural coloring matter, Carminic acid, a laccainic acid, cull SAMIN, brazilin, crocin, etc. are mentioned, these granular materials may be composite-ized or oils, silicone, or a fluorine compound may perform a surface treatment.

[0030]As alcohols, lower alcohol, such as ethanol and isopropanol, Polyhydric alcohol, such as glycerin, diglycerol, ethylene glycol, a diethylene glycol, triethylene glycol, propylene glycol, dipropylene glycol, a 1,3-butylene glycol, and a polyethylene glycol, etc. are mentioned.

[0031]As a water soluble polymer, gum arabic, tragacanth, galactan, Carob gum, guar gum, karaya gum, a carrageenan, pectin, Vegetable system polymers, such as agar, ARUGE colloid, tolan TOGAMU, locust bean gum, and galactomannan, Microorganism system polymers, such as xanthan gum, dextran, SAKUSHINO glucan, and pullulan, Animal system polymers, such as casein, albumin, and gelatin, starch, carboxymethyl starch, Starch system polymers, such as methyl hydroxypropyl starch, methyl cellulose, Ethyl cellulose, methyl hydroxypropylcellulose, carboxymethyl cellulose, Hydroxymethylcellulose, hydroxypropylcellulose, a nitrocellulose, Cellulose sodium sulfate, carboxymethylcellulose sodium, Crystalline cellulose, the cellulose type polymers in the end of cellulose, sodium alginate, Alginic acid system polymers, such as propylene glycol alginate, Vinyl system polymers, such as polyvinyl methyl ether, a carboxyvinyl polymer, and an alkyl modification carboxyvinyl polymer, polyoxyethylene system polymers, polyoxyethylene polyoxypropylene copolymer system polymers, There are inorganic system water soluble polymers, such as acrylic polymers, such as sodium polyacrylate, polyethylacrylate, and polyacrylamide, polyethyleneimine, cation polymer, bentonite, RAPONAITO, and hectorite, resin, a clathrate, etc. In this, coat formation agents, such as polyvinyl alcohol and a polyvinyl pyrrolidone, are also contained.

[0032]As an antimicrobial agent, benzoic acid, sodium benzoate, carbolic acid, sorbic acid, Sorbic acid potassium salt, a paraoxybenzoic acid, the PARAKURORU metacresol, Hexachlorophene, a benzalkonium chloride, chloridation chlorhexidine, trichlorocarbanilide, sensitization matter, bis(2-pyridylthio 1-oxide)zinc, phenoxyethanol, thianthol, isopropylmethyl phenol, etc. are mentioned.

[0033]As a pH adjuster, sodium acid citrate, such as potassium carbonate, sodium bicarbonate, and ammonium acid carbonate, malic acid sodium, a sodium oxalate, etc. are mentioned.

[0034]As a pick-me-up, L-menthol, camphor, its derivative, etc. are mentioned.

[0035]As a circulation accelerator, nicotinic acid, nonylic acid WARENIRU amide, capsaicin, A zingerone, cantharides tincture, ichthammol, alpha-borneol, Inositol hexanicotinate, cyclandelate,

cinnarizine, tolazoline, acetylcholine, verapamil, a ribonucleic acid decomposition product, a xanthin, caffeine, \*\*-oryzanol, those derivatives, etc. are mentioned.

[0036]As a skin astringent, lipase, papain, etc. are mentioned as enzymes, such as a triane trawl, as antiseborrheic drugs, such as tannic acid.

[0037]As a whitening agent, vitamin C, its derivative and those salts, a placenta extract, Licorice extract containing glove lysine, glabrene, Ricou Jiri Ching, isoRIKUIRICHIN, and these, A coix seed extract, a Scutellaria root extract, a seaweed extract, the Ampelopsis japonica extract, A SEMPUKUKA extract, a grape extract, wheat extract, a tomato extract, astaxanthin, The animals-and-plants extract, agarose, oligosaccharide containing carotenoid and these, Neo agarobiose, hydroquinone, its derivative, and those salts, Cystein, its derivative and those salts, an asparagus extract, An acerola extract, Bistorta major extract, the Rose Fruit extract, a Siberian ginseng extract, Endothelin antagonists, such as a green-peas extract and a chamomile extract, a cam cam extract, The Spatholobus suberectus Dunn extract, an orange extract, a bramble extract, a kiwi extract, The vegetable oil containing linolic acid, such as a sophorae radix extract, a coffee extraction thing, sesame, and sesame, A GOKAHI extract, a rice bran extract, a wild ginger extract, a white thorn extract, a SAMPENZU extract, a peony extract, a sila lily extract, the Mulberry bark extract, an angericae radix extract, a beech extract, the bud extract of Buna, a blackcurrant extract. Tea extracts, such as garden balsam extract, hop extract, a mica cuttlefish extract, a Chinese quince extract, a creeping saxifrage extract, oolong tea, tea, and green tea, a Ganoderma extract, microorganism fermentation metabolite, a soybean extract, a molasses extract, a rakanka extract, etc. are mentioned.

[0038]As hormone, melatonin and its derivative, adenocorticotrophic hormone and its derivative, phytohormones (auxin, cytokinin, gibberellin, kinetin, abscisic acid, ethylene, etc.), the derivative of those, etc. are raised. as vitamins -- vitamin A and its derivative (retinol palmitate.) Retinal, its derivatives, etc., such as retinols, such as retinol acetate, and a derivative of those, and dehydroretinal, vitamin B and its derivative (thiamine hydrochloride, thiamin sulfate, and riboflavin.) Acetic acid riboflavin, pyridoxine hydrochloride, pyridoxine dioctanoate, Flavin adenine dinucleotide, cyanocobalamine, folic acid, nicotinamide, Those salts [, such as nicotinic acid and Kolin ], such as nicotinic acid benzyl, vitamin C and its derivative (L-ascorbic acid phosphoric ester and L-ascorbyl sulfate.) Dipalmitate L-ASUKORUBIRU and L-ascorbic acid 2-glucoside, those salts, such as tetraisopulmitic acid L-ASUKORUBIRU, vitamin D, and its derivative (ergocalciferol.) alpha-, such as cholecalciferol and a dihydroKISHISUTA knurl, and gamma-linolenic acid, The derivatives and those salts, such as nicotinamide, are raised as essential fatty acid, such as linolic acid and fatty acid of omega-3 system, and those derivatives, and other vitamins. [, such as nicotinic acid, biotin, and inositol, ] As a keratolytic drug, organic acid, such as AHA(s), such as citrate, lactic acid, tartaric acid, malic acid, glycolic acid, and succinic acid, and salicylic acid, is raised.

[0039]As vegetation and an animal, and an extract from microorganism, an almond (extract of vegetable origin) extract, A rosemary extract, a malt root extract, an asparagus extract, an apricot extract, A ginkgo tree extract, a cork tree bark extract, a barley extract, a kiwi extract, A cucumber extract, a shiitake mushroom extract and its decomposition product, or those derivatives, A field horsetail extract, a lettuce extract, a lemon extract, a sialid extract, glutamic acid, A soybean extract, a zizyphi fructus extract, the Centella asiatica extract, theanine, a red pepper extract, The Calendula officinalis extract, a tomato extract, a garlic extract, a Hoelen extract, The extract of vegetable origin etc. which are chosen from the bud extract of Buna, a peach extract, a eucalyptus extract, a lily bulb extract, a grape-seeds oil, etc.,

(Extract of animal origin) Mollusk extracts, such as a silk protein, royal jelly, and a sepia, Crest extracts, such as a shell extract, a shell meat extract, and a fish meat extract, a blood serum deproteinization extract, The extract etc. which are chosen from an extract from microorganism or fermentation metabolite, such as a yeast extract (extract from microorganism), lactoferrin or its decomposition products, such as placenta extracts, such as a swine and a cow, a lactic-acid-bacteria extract, a lactobacillus bifidus extract, and a Ganoderma extract, are mentioned.

[0040]As a moisturizer, hyaluronic acid, chondroitin sulfate, dermatan sulfate, Mucopolysaccharides or those salts, such as a heparan sulfate, heparin, and a keratan sulfate, Protein or those derivatives, such as collagen, elastin, fibronectin, and keratin, Hydrolyzates and those salts, a glycine, an alanine, valine, isoleucine, Serine, threonine, aspartic acid, glutamic acid, asparagine, Glutamine, lysine, hydroxylysine, arginine, cystein, Cystine, methionine, phenylalanine, tyrosine, proline, theanine, An amino acid derivative or its salts, such as hydroxyproline, ORUCHININ, citrulline, and pyrrolidone carboxylic acid, Sorbitol, erythritol, malt sugar, maltitol, xylitol, Sugars, such as xylose, trehalose, inositol, glucose, mannitol, pentaerythritol, fructose, sucrose and its ester, dextrin and its derivative, and honey, mucin, urea, phospholipid, a glycolipid, ceramide, etc. are mentioned.

[0041]

[The example of an examination, and an example] Next, although the example of an examination and an example are given and this invention is explained still in detail, this invention is not restrained at all by these.

[0042]Example of examination 1 Fibroblast NB1RGB of the optical aging inhibition test Homo sapiens newborn infant origin by a cell culture was used. A proper quantity of culture media were taken on the petri dish, seeding of the fibroblast NB1RGB was carried out, and it settled in 37 \*\* and 5% of carbon dioxide levels. On the next day, it added in the culture medium by making acetylation L-histidine, L-histidine, rutin, quercetin, mannitol, a mica cuttlefish extract, dehydroretinal, and a Betula-alba extract into a sample. In acetylation L-histidine, L-histidine, rutin, quercetin, mannitol, and dehydroretinal, addition concentration added and mixed specimen preparation liquid so that the last concentration might serve as 0 (contrast) and 10mM. On the other hand, the mica cuttlefish extract and the Betula-alba extract added and mixed specimen preparation liquid so that the last concentration in a culture medium might be 0.01 and 0.05% respectively. It irradiated with UV-A with the UV irradiation machine, and specimen preparation liquid was added again. This operation was performed a total of 3 times every other day every week. In order to plant and inherit, the cell was processed with trypsin 0.25%, after a phosphate buffer solution washed, it separated the cell, and were collected by the culture medium of the specified quantity every week. After measuring a cell number, seeding of the 1/4 whole quantity was carried out to the petri dish into which optimum dose of culture media of the same type were put. Thus, 1 time of a cell planted every week, and a splice and three UV-A exposures were continued until it resulted in the stop of division of a cell.

[0043](Valuation basis) From the number of seeding of a cell, and the cell number collected after culture, it asks for a cell population's number (PDL) of doubling, and uses as an index of cellular life span. It asks for a cell population's number of doubling by the following formula (1), it accumulates the result for every passage, and computes it as a cell population doubling number.

[Equation 1]Cell population doubling number (PDL) = $\text{Log}(\text{recovery cell number} / \text{seeding cell number}) / \text{Log}2$  [0044]( Result)

[Table 1]



	処理検体	濃度	最終 PDL
本発明品	アセチル化 L-ヒスチジン * 1	10 mM	66.3
	L-ヒスチジン * 2	10 mM	65.4
	ルチン * 3	10 mM	64.2
	クエルセチン * 4	10 mM	62.1
	マンニトール * 5	10 mM	60.1
	マイカイカ抽出液 * 6	0.01%	59.7
比較品	デヒドロレチナール * 7	10 mM	57.1
	シラカバ抽出液 * 8	0.05%	55.4
	無添加	-	56.5

- |            |            |
|------------|------------|
| * 1 シグマ社製  | * 5 和光純薬社製 |
| * 2 和光純薬社製 | * 6 丸善製薬社製 |
| * 3 東洋精糖社製 | * 7 シグマ社製  |
| * 4 東京化成社製 | * 8 丸善製薬社製 |

[0045]It was admitted that the optical aging depressant of this invention had a high anti-aging operation to shortening of the cell division life by UV-A of fibroblast NB1RGB of the Homo sapiens newborn infant origin so that clearly from the result of Table 1. Therefore, by applying the ingredient concerned which has singlet oxygen elimination ability to skin, the extremely outstanding anti-aging operation can be demonstrated and generating of the wrinkles of the skin produced by chronic ultraviolet-rays exposure etc., slack, etc. can be prevented effectively.

[0046]Example 1 cream: The cream which contains an optical aging depressant by the presentation and the following process which are shown in Table 2 was prepared, and the wrinkles improvement effect in an optical aging (optical aging) mouse was investigated. This result is written together to Table 2.

[0047](A presentation and a result)

[Table 2]

	成 分 (%)	本発明品		比較品	
		1	2	1	2
(1)	ミツロウ	6.0	6.0	6.0	6.0
(2)	セタノール	5.0	5.0	5.0	5.0
(3)	還元ラノリン	5.0	5.0	5.0	5.0
(4)	スクワラン	30.0	30.0	30.0	30.0
(5)	親油型モノステアリン酸グリセリル	4.0	4.0	4.0	4.0
(6)	ポリオキシエチレンソルビタン モノラウレート (20E.O.)	2.0	2.0	2.0	2.0
(7)	L-ヒスチジン * 1	0.5	—	—	—
(8)	アセチル化 L-ヒスチジン * 2	—	0.5	—	—
(9)	デヒドロレチナール * 3	—	—	1.0	—
(10)	防腐剤	適量	適量	適量	適量
(11)	香料	適量	適量	適量	適量
(12)	精製水	残量	残量	残量	残量
	シワ改善効果	1.8	2.2	1.3	0.5

\* 1 和光純薬社製

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\* 3 シグマ社製

[0048]( Process)

A. Mix and heat ingredient (1) - (6) and (9) - (11), and keep at 70 \*\*.

B. Heat a part of ingredient (12) and keep at 70 \*\*.

C. B was added to A, it cooled and cream was obtained, after mixing (7) dissolved with the remainder of (12), and (8).

(Test method) Preliminary breeding of the hairless-mouse (HOS/HR-1) 6 weeks-old female is carried out for one week for acclimatization. The experiment processing group of ten per subject cream is set up, and it irradiates with UV by the intensity of 0.1 J/cm<sup>2</sup> after one week every day. Subject cream was back applied at a rate of 0.1 g/cm<sup>2</sup> over 2 times, a morning and night, and 20 weeks every day. Before an exposure, the regions-of-back skin is wiped and extant cream is removed. The following standards estimated the wrinkle improvement effect by spreading, and it computed as the average mark of the score of each mouse.

[0049]

(Valuation basis)

<evaluation> score Inside of < \*\* > -- very effective There are almost no wrinkles of 3 skin. an owner -- Effect The wrinkles of 2 skin are seldom conspicuous. Slightly effective The wrinkles of 1 skin are a little conspicuous.

Wrinkles are conspicuous to invalidity 0 skin.[0050]It was admitted that L-histidine and acetylation L-histidine had high generation-of-crease depressor effect to the generation control of an optical degraded phenomenon mouse in back so that clearly from the result of Table 2. Therefore, by applying the ingredient concerned to skin, the extremely outstanding anti-light ageing action can be demonstrated, and generating of the wrinkles of the skin produced by chronic ultraviolet-rays exposure etc., slack, etc. can be prevented effectively.

[0051]Example 2 cream: The cream which contains an optical aging depressant by the presentation and the following process which are shown in Table 3 was prepared, and the wrinkles improvement effect in a panel test was investigated. This result is written together to Table 3.

[0052](A presentation and a result)

[Table 3]

	成 分 (%)	本発明品			比較品	
		1	2	3	1	2
(1)	ミツロウ	6.0	6.0	6.0	6.0	6.0
(2)	セタノール	5.0	5.0	5.0	5.0	5.0
(3)	還元ラノリン	5.0	5.0	5.0	5.0	5.0
(4)	スクワラン	30.0	30.0	30.0	30.0	30.0
(5)	親油型モノステアリン酸グリセリル	4.0	4.0	4.0	4.0	4.0
(6)	ポリオキシエチレンソルビタンモノラウレート (20E.O.)	2.0	2.0	2.0	2.0	2.0
(7)	L-ヒスチジン * 1	0.5	—	—	—	—
(8)	アセチル化L-ヒスチジン * 2	—	0.5	—	—	—
(9)	マンニトール * 3	—	—	0.5	—	—
(10)	デヒドロレチナール * 4	—	—	—	1.0	—
(11)	防腐剤	適量	適量	適量	適量	適量
(12)	香料	適量	適量	適量	適量	適量
(13)	精製水	残量	残量	残量	残量	残量
効シ 果ワ 改 善	有 効	7	7	5	2	0
	やや有効	3	2	4	3	2
	無 効	0	1	1	5	8

\* 1 和光純薬社製

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\* 3 和光純薬社製

- \* 2 シグマ社製
- \* 3 和光純薬社製
- \* 4 シグマ社製

[0053]( Process)

A. Mix and heat ingredient (1) - (6) and (10) - (12), and keep at 70 \*\*.

B. Heat a part of ingredient (13) and keep at 70 \*\*.

C. B was added to A, it cooled and cream was obtained, after mixing (7) - (9) dissolved with the remainder of (13).

(Test method) Ten women aged [ per subject cream ] from 40 to 59 were used as the panel, and the optimum dose of subject cream was applied to the face after washing its face over 2 times, a morning and night, and 20 weeks every day. The following standards estimated the wrinkle improvement effect by spreading.

[0054](Valuation basis)

inside of <evaluation> < \*\*> -- an owner -- Effect The wrinkle of skin stopped being conspicuous.

Slightly effective The wrinkle of skin stopped being not much conspicuous.

Nothing With an effect use front and no change.

[0055]As shown in the result of Table 3, the cream of this invention article 1 which blended L-histidine and this invention article 2 which blended acetylation L-histidine, and this invention article 3 which blended mannitol, By applying these to the skin, the wrinkles of skin have been improved and it became clear to consider it as a beautiful skin with tension.

[0056]Example 3 cream: Cream was prepared by the presentation and the following process which are shown in Table 4 and 5, and the wrinkle improvement effect at the time of using together L-histidine, rutin glucoside, an anti-oxidant, a moisturizer, a chelating agent, and ultraviolet inhibitor was investigated. This result is shown in Table 4 and 5.

[0057](A presentation and a result)

[Table 4]

	成 分 (%)	本発明品					
		4	5	6	7	8	9
(1)	ミツロウ	4.0	4.0	4.0	4.0	4.0	4.0
(2)	セタノール	5.0	5.0	5.0	5.0	5.0	5.0
(3)	還元ラノリン	5.0	5.0	5.0	5.0	5.0	5.0
(4)	スクワラン	20.0	20.0	20.0	20.0	20.0	20.0
(5)	親油型モノステアリン酸グリセリル	4.0	4.0	4.0	4.0	4.0	4.0
(6)	ポリオキシエチレンソルビタンモノラウレート (20E.O.)	2.0	2.0	2.0	2.0	2.0	2.0
(7)	Ｌ－ヒスチジン *1	0.5	0.10	0.10	0.10	0.10	0.10
(8)	ルチングルコシド *2	—	0.12	—	—	—	—
(9)	パルミチン酸レチノール *3	—	—	0.25	—	—	—
(10)	コンフリー抽出液 *4	—	—	—	0.05	—	—
(11)	フィチン酸 *5	—	—	—	—	0.05	—
(12)	パラメトキシケイ皮酸－2－エチルヘキシル*6	—	—	—	—	—	0.25
(13)	防腐剤	適量	適量	適量	適量	適量	適量
(14)	香料	適量	適量	適量	適量	適量	適量
(15)	精製水	残量	残量	残量	残量	残量	残量
シ 効 ワ 果 改 善	有 効	7	9	7	7	6	8
	やや有効	3	1	2	3	4	1
	無 効	0	0	1	0	0	1

\*1 和光純薬社製

\*4 一丸ファルコス社製

\*2 東洋精糖社製

\*5 三井化学社製

\*3 日本ロシュ社製

\*6 BASF社製

[0058]

[Table 5]

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\* 3 日本ロシュ社製

\* 6 BASF社製

[http://www4.ipdl.inpit.go.jp/cgi-bin/tran\\_web.cgi\\_ej...0000000000000000&N0550=11111110111000000000&N0580=0](http://www4.ipdl.inpit.go.jp/cgi-bin/tran_web.cgi_ej...0000000000000000&N0550=11111110111000000000&N0580=0) (14 of 16)12/9/2008 3:18:29 PM

article 4 which blended L-histidine, and this invention article 5 which blended rutin guru KOTOSHIDO with L-histidine has improved the wrinkle of skin, and became clear [ considering it as a beautiful skin with tension ]. By applying to the skin the external preparations which used together and blended L-histidine, an anti-oxidant, a moisturizer, a chelating agent, and ultraviolet inhibitor, The wrinkle improvement effect of a skin more outstanding compared with the case where the external preparations which blended L-histidine independently are applied was demonstrated synergistically, and it became clear to consider it as a beautiful skin with tension.

[0063]

Example 4 (%) Face toilet : (formula)

(1) glycerin 5.0(2)1,3-butylene glycol . 6.5 (3) polyoxyethylenes (20E.O.) 1.2 Sorbitan mono- laurate ester (4) ethyl alcohol 8.0 (5) L-histidine\*1 0.3 (6) antiseptics Optimum dose (7) perfume Optimum dose (8) purified water Residue \*1 Wako Pure Chem make[0064]( Process)

A. Carry out the mixture solution of an ingredient (3), (4), (6), and (7).

B. Carry out the mixture solution of an ingredient (1), (2), (5), and (8).

C. A and B were mixed, it was made uniform and face toilet was obtained.

[0065]

Example 5 (%) Milky lotion (formula)

(1) Polyoxyethylene (10E.O.) 1.0 A sorbitan monostearate (2) polyoxyethylene (60E.O.) Sorbitol tetra oleate 0.5(3) glyceryl monostearate 1.0 (4) stearic acid 0.5 (5) behenyl alcohol 0.5 (6) squalane 8.0(7) hydrogenation soybean phosphatide \*1 0.5 (8) retinol-palmitate \*2. 0.5 (9) acetylation L-histidine\*3. 1.0 (10) sodium-acid-citrate \*4 The 0.15 (11) antiseptic 0.1 (12) carboxyvinyl polymer 0.1 (13) sodium hydroxide 0.05 (14) ethyl alcohol 5.0 (15) purified water Residue (16) perfume . Optimum dose \*1 Nikko Chemicals \*2 Nippon Roche make \*3 Sigma company make \*4 Nippon Roche make [0066]( Process)

A. Ingredient (13) Heating mixing of - (15) is carried out, and it keeps at 70 \*\*.

B. Ingredient (1) Heating mixing of - (8) and (11) is carried out, and it keeps at 70 \*\*.

C. Add A to B, mix and emulsify uniformly.

D. (9), (10), (12), and (16) were added after cooling, C was mixed uniformly, and the milky lotion was obtained.

[0067]Example 4 and Example 5 were the face toilet and the milky lotions which are used as a beautiful skin which improves the wrinkle of skin and slack by aging and has tension by each being excellent in temporal stability and applying to the skin.

[0068]

Example 6 (%) Ointment (formula)

(1) stearic acid 18.0 (2) cetanols . 4.0 (3) triethanolamines 2.0 (4) glycerin . 5.0(5) YASHAJITSU extract \*1 0.5 (6) acetic-acid dl-\*\*-tocopherol\*2 0.25(7) Para methoxycinnamic acid-2-ethylhexyl \*3 2.5 (8) purified water Residue \*1 ICHIMARU PHARCOS CO., LTD. make \*2 Eisai Co., Ltd. make \*3 BASF A.G. make[0069]( Process)

A. Carry out heating mixing of a part of ingredient (3), (4), and (8), and keep at 75 \*\*.

B. Carry out heating mixing and keep the ingredient (1), (2), and (7) at 75 \*\*.

C. Add A to B gradually.

D. (5) dissolved with the remainder of (8) and (6) were added cooling C, and ointment was obtained.

[0070]Example 6 was ointment used as a beautiful skin which improves the wrinkle of skin, and slack and

has tension by excelling in temporal stability and applying to the skin.

[0071]

Example 7 (%) Pack (formula)

(1) Polyvinyl alcohol 20.0 (2) ethyl alcohol 20.0 (3) glycerin 5.0 (4) kaolin 6.0 (5) rutin sugar derivative \*1 1.0 (6) SAMPENZU extract \*2 2.0 (7) comfrey extract \*3 3.0 (8) phytic-acid \*4 0.05 (9) antiseptics 0.2 (10) perfume 0.1 (11) purified water Residue \*1 TOYO SUGAR REFINING CO., LTD. make \*2 Maruzen Pharmaceuticals Co., Ltd. make \*3 ICHIMARU PHARCOS CO., LTD. make \*4 Mitsui Chemicals, Inc. make [0072] (Process)

A. Mix an ingredient (1), (3), (4), (8), and (11), and heat and agitate at 70 \*\*.

B. Mix the ingredient (2) and (9).

C. The above-mentioned B was added to previous A, after mixing, it cooled, (5) - (7) and (10) were distributed uniformly, and the pack was obtained.

[0073] Example 7 was a pack used as a beautiful skin which improves the wrinkle of skin, and slack and has tension by excelling in temporal stability and applying to the skin.

[0074]

Example 8 (%) Facial liquid foundation : (formula)

(1) lanolin 7.0 (2) liquid paraffins . 5.0 (3) stearic acid 2.0 (4) cetanols . 1.0 (5) nicotinamide \*1 2.0 (6) Para methoxycinnamic acid 3.0-2-ethylhexyl \*2 (7) glycerin 5.0 (8) triethanolamines 1.0 (9) carboxymethyl cellulose 0.7 (10) purified water . Residue (11) titanium oxide \*38.0 (12) particulate-titanium-oxide \*4 2.0 (13) zinc-oxide \*5 5.0 (14) mica 15.0 (15) talc 6.0 (16) color pigments 6.0 (17) astaxanthin \*6 0.01 (18) citrate \*7 0.1 (19) perfume Optimum dose \*1 organic-synthesis medicine company make \*2 BASF company make \*3 TAYCA CORP. make \*4 TAYCA CORP. make \*5 Sakai chemicals company make \*6 ITANO REFRIGERATED FOOD Co., Ltd. make \*7 Wako Pure Chem make [0075] (Process)

A. Ingredient (1) The mixture solution of - (6) is carried out.

B. Add ingredient (11) - (16) to A, mix uniformly, and keep at 70 \*\*.

C. Ingredient (7) - (10) is dissolved uniformly and it keeps at 70 \*\*.

D. Add C to B and emulsify uniformly.

E. Ingredient (17) - (19) was added for D after cooling, and facial liquid foundation was obtained.

[0076] Example 8 was facial liquid foundation which improves the wrinkle of skin and slack by aging etc. by excelling in temporal stability and applying to the skin.

[0077]

[Effect of the Invention] Like the above, the skin external preparations containing the optical aging depressant and \*\*\*\*\* of this invention have the anti-aging effect, demonstrate a high improvement effect to wrinkles, and are effective in the wrinkle of the skin by aging and ultraviolet-rays exposure, an improvement of slack, etc. The skin external preparations of this invention which blended other medicinal properties, such as an anti-oxidant, a moisturizer, a chelating agent, and ultraviolet inhibitor, have the anti-aging effect more outstanding compared with the case where the optical aging depressant of this invention is blended independently. Therefore, the skin external preparations containing the optical aging depressant and \*\*\*\*\* of this invention can be advantageously used as cosmetics aiming at aging prevention, drugs, etc.